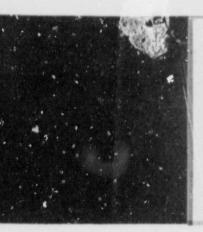
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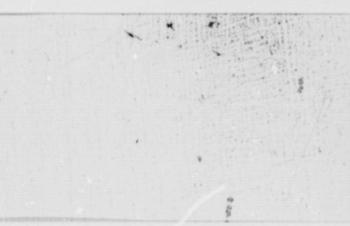
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# NATIONAL BIOMEDICAL RESEARCH FOUNDATION

GEORGETOWN UNIVERSITY MEDICAL CENTER
3900 RESERVOIR ROAD, N. W.
WASHINGTON, D. C. 20007
202-625-2121

FINAL TECHNICAL REPORT

NASA CONTRACT NASW3317

9/1/79 - 12/31/83

### FINAL REPORT

for

NASA Contract NASW 3317

Investigation of Compounds Essential for the Origin of Life

> covering the period 9/1/79 to 12/31/83

### Principal Investigators

Margaret O. Dayhoff, Ph.D. Sept. 1979 to Feb. 1983

Lois T. Hunt, Ph.D.

Feb. 1983 to Dec. 1983

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- 3. P.R. 4/22/83 for the period 9/1/81 12/31/82
- 4. P.R. 4/27/84 for the period 1/1/83 12/31/83

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### INTRODUCTION

The enclosed annual progress reports and publications describe and document the research performed by us with the support of NASA contract NASW 3317. This contract extended over a period characterized by intense activity and startling discoveries in the interrelated areas of molecular biology, genetics, and evolutionary studies of prokaryotes, eukaryotes, and their viruses.

### PROPOSAL AND PROGRESS REPORT &

INVESTIGATION OF COMPOUNDS ESSENTIAL FOR THE ORIGIN OF LIFE NASW 3317

National Biomedical Research Foundation Georgetown University Medical Center 3900 Reservoir Road Washington, D.C. 20007

August 28, 1980

Principal Investigator Margaret O. Dayhoff, Ph.D. Co-principal Investigator Robert M. Schwartz, Ph.D.

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- G. Protein Segment Dictionary 78, M.O. Dayhoff, L.T. Hunt, W.C. Barker, R.M. Schwartz, and B.C. Orcutt, National Biomedical Research Foundation, Washington, D.C., 1978, 470 pp.
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### II. PROGRESS REPORT 1/1/78 - 8/25/80

### Introduction

In early 1978, we published an article in Science that synthesized all of the available sequence data pertinent to bacterial and blue—green evolution and to the origin of eukaryote organelles. The articles in press from the 6th International Conference on the Origins of Life together with that in press from the International Colloquium on Endosymbiosis and Cell Research (see Section II-D) update that study. They suggest that the origin of the eukaryote organelles, the mitochondria and the chloroplasts, were not only endosymbiotic but also polyphyletic, i.e., organelles in different lines of descent arose from different bacteria or blue—greens.

The paper submitted to Nature with Dr. Barnabas initiated a new line of interest for us. In that work we correlated the metabolic capabilities of bacterial groups for which sequence data are available with their evolutionary position based on the sequence data. From this, we begin to infer the order in which a variety of metabolic pathways developed during the Precambrian. These metabolic capabilities include fermentation, anaerobic respiration, bacterial anoxygenic photosynthesis, sulfate reduction, aerobic respiration, and oxygenic photosynthesis.

Recent breakthroughs in DNA and RNA sequencing techniques have greatly speeded the elucidation of these sequence data. Much of the new data is a natural adjunct to our protein data collection, particularly the sequences of complete genomes, genes, and messenger RNAs. Other sequences, although less direct in their connection, are still extremely important, for example, control signals, ribosomal-binding sites, and origins of replication. During the last year, we have developed a computerized nucleic acid sequence data base and programs for data entry and retrieval as a demonstration project. Our demonstration project has as its goal showing what is necessary to make this new detailed genetic data intellectually accessible. In the first section of this report, we have included items describing the current state of our data base:

1. An editorial that appeared in Nature pointing out the need for such a



data base and our reply to that editorial.

- 2. A letter to be published in Science announcing the public availability of our data base.
- 3. Computer terminal display for our demonstraton system.
- 4. A table of contents of the data base as it currently stands as well as a sample of the data entries. Anythereof they have yellowhere with

IF ANY MEMBERS OF THE GROUP REVIEWING THIS PROPOSAL WOULD LIKE ACCESS TO OUR NUCLEIC ACID SEQUENCE REFERENCE DATA BASE, THEY MAY CALL EITHER DR. DAYHOFF OR DR. SCHWARTZ AT (202) 625-2121.

Clearly, making the data accessible is only the first step in the research process. Our NASA contract has supported that portion of this data collection bearing on origin of life studies. Additionally, we have requested supplemental funds to support one senior staff member during the four months the demonstration project will be on line in order to help update the retrieval system and modify our programs in response to user needs.

We have continued to maintain a reference data collection of protein sequences. Our NASA contract supports that part of the data collection and analysis that is of interest to the study of the origin and early evolution of life. In 1979, we published supplement 3 to volume 5 of the Atlas of Protein Sequence and Structure and a Protein Segment Dictionary (both submitted separately). We are currently working toward the publication of volume 6 of the Atlas at the end of 1982. This will be a comprehensive book including new data as well as combining and updating the information in volume 5 and its three supplements. A list of the new protein data arranged hierarchically by evolutionary relationship is shown in Section II-E.

### List of Publications 1/1/78 - 8/25/80

### Books Published:

Atlas of Protein Sequence and Structure, Vol. 5, Suppl. 3, ed. M.O. Dayhoff, National Biomedical Research Foundation, Washington, D.C., 1978, 414 pp.

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Protein Segment Dictionary 78, M.O. Dayhoff, L.T. Hunt, W.C. Barker, R.M. Schwartz and B.C. Orcutz, National Biomedical Research Foundation, Washington, D.C., 1978, 470 pp.

### Other Output:

Protein sequence Data Tape, Atlas of Protein Sequence and Structure, M.O. Dayhoff, L.T. Hunt, W.C. Barker and R.M. Schwartz, National Biomedical Research Foundation, Washington, D.C., 1978. [119,006 residues from 1,081 sequences]

### Papers Published:

An outline of biological evolution based on macromolecular sequences. R.M. Schwartz, M.O. Dayhoff. COMPARATIVE PLANETOLOGY, ed. by C. Ponnamperuma, pp. 225-242. Academic Press, N.Y., 1978.

Origins of prokaryotes, eukaryotes, mitochondria, and chloroplasts. R.M. Schwartz and M.O. Dayhoff, <u>Science</u> 199: 395-403, January 27, 1978.

The point mutation process in proteins. R.M. Schwartz and M.O. Dayhoff, in: Origin of Life: Proceedings of the Second ISSOL Meeting, the Fifth ICOL Meeting, Haruhiko Noda, editor, Center for Academic Publications Japan/Japan Scientific Societies Press, 1978, pp. 457-469.

Evolution of early life inferred from protein and ribonucleic acid sequences. M.O. Dayhoff and R.M. Schwartz, in: Origin of Life: Proceedings of the Second ISSOL Meeting, the Fifth ICOL Meeting, Haruhiko Noda, editor, Center for Academic Publications Japan/Japan Scientific Societies Press, 1978, pp. 547-560.

Detection of distant relationships based on point mutation data. R.M. Schwartz and M.O. Dayhoff, Evolution of Protein Moleculaes, ed. H. Matsubara and T. Yamanaka, pp. 1-16. Center for Academic Publications Japan/Japan Scientific Societies Press, Tokyo, 1978.

Evolution of prokaryotes inferred from sequences. M.O. Dayhoff and R.M. Schwartz, Evolution of Protein Molecules, ed. H. Matsubara and T. Yamanaka, pp. 323-42. Center for Academic Publications Japan/Japan Scientific Societies Press, Tokyo, 1978.

Protein and nucleic acid sequence data and phylogeny. R.M. Schwartz and M.O. Dayhoff. Science 205 (4410): 1036-39, 7 Sept. 1979. [Exchange of Technical Comments with Vincent Demoulin]

Evolutionary relationships among photosynthetic prokaryotes inferred from protein and nucleic acid sequence data. R.M. Schwartz and M.O. Dayhoff. Third International Symposium on Photosynthetic Prokaryotes, Oxford, 1979. Abstracts. E7

Prokaryote evolution and the symbiotic origin of eukaryotes. M.O. Dayhoff and R.M. Schwartz. Proceedings of the International Colloquium in Endosymbiosis and Cell Research, April 11-15, 1980, Tubingen, Germany. Berlin: Walter deGruyter & Co., 1980. In press.

Phylogenetic sequence of metabolic pathways in precambrian cellular life. J. Barnabas, R.M. Schwartz, and M.O. Dayhoff. Proceedings of the 6th International Conference on the Origins of Life. Dordrecht, The Netherlands: Reidel, 1980. In press.

The evolution of Liue-greens and the origins of chloroplasts. R.M. Schwartz and M.O. Dayhoff. Proceedings of the 6th International Conference on the Origins of Life. Dordrect, The Netherlands: Reidel, 1980. In press.

Evolution of the rhodospirillaceae and mitochondria: a view based on sequence data. M.O. Dayhoff and R.M. Schwartz. Proceedings of the 6th International Conference on the Origins of Life. Dordrecht, The Netherlands: Reidel, 1980. In press.

Paper submitted for publication:

Evolution of major metabolic innovations in the precambrian. J. Barnabas, R.M. Schwartz, and M.O. Dayhoff. Submitted to <u>Nature</u>, June 1980.

New Entries and Their Protein Superfamilies Up-date of May 1980

M.O. Dayhoff, H.R. Chen, B.C. Orcutt, W.C. Barker, L.T. Hunt, and R.M. Schwartz

NBR Report 08710-800515

National Biomedical Research Foundation

Georgetown University Medical Center

3900 Reservoir Road, N.W.

Washington, D.C. 20007

### CONTENTS

- 1. Superfamily list from the Atlas, Suppl. 3, containing the complete, sequences.
- 2. Explanation of computer listings of new entries.
- 3. Computer listing of new, complete or almost complete sequences with their superfamily classification.
- 4. Alphabetical listing of other new entries.

# 2 Protein Superfamilies

M.O. Dayhoff, W.C. Barker, L.T. Hunt, and R.M. Schwartz

In the list that follows, we have organized all of the complete sequences reported in the *Atlas* volumes into groups of superfamilies, families, subfamilies, and entries. The number in each group, the criteria for clustering, and the method of identification of the hierarchical levels in the list are shown below.

Number of		Criteria for Clustering	Identifica- tion of
Groups	Group	Sequences	Cluster
181	Superfamilies	Probability of similarity by chance < 10 <sup>-6</sup>	Number
314	Families	<50% different	Letter
537	Subfamilies	< 20% different	Paragraph
793	Atlas entries	< 5% different	Semicolon
Sequences	In the same and	# / are separated b	y commas.

This list updates the that appeared in Supplement 2,1 in which there were 116 superfamilies, 197 families, 328 subfamilies, and 493 entries. There has been about a 60% increase in all categories in the intervening 2 years and 7 months.

Only complete or nearly complete sequences that are 20 or more residues in length are included. The constant and variable regions of immunoglobulins are counted as separate sequences. Sequences that can be considered complete in one sense but partial in another are generally included. Examples are active hormone and enzyme sequences that are derived from longer precursors, and sequences of entire homology regions from proteins with two or more such regions.

Proteins within a family usually differ at fewer than half of their amino acid positions and they are either homologs in various species or products of gene duplication; their similarity of function has usually been recognized before the sequences were known and they have identical or very similar names. Families are identified by letters in the list.

The sequences within a family have been divided into subfamilies, which are shown as paragraphs. Sequences within a subfamily usually differ from each other at fewer than 20% of their amino acid positions. Within a subfamily, sequences that differ by less than 5% and form a single

Atlas entry are separated by commas, whereas sequences or groups that are more than 5% different are separated by semicolons,

In a clustering procedure such as this there will always be cases that are borderline, some pairs within a group being below the cutoff and some above. Where possible, we have grouped together proteins that fall on the same branch of an evolutionary tree.

The families are grouped into superfamilies,2,3 idenrified by numbers, where similarity of sequences in different families can be recognized by statistical procedures. We have used two such methods to compare pairs of complete sequences; for sequences of comparable length we used a method based on the best alignment of the two sequences; for sequences of quite different length, we used a method based on the distribution of scores obtained on comparison of all segments of a given length from one sequence with those from the other. These methods are described in detail in chapter 1. Each method produces a probability that the scores from the comparison of two real sequences could have been derived from the distribution of scores produced by comparisons of pairs of randomly permuted sequences with the same amino acid compositions as the two real sequences.

A newly determined sequence is placed in an existing superfamily if, on comparison with the best conserved sequence from each family in that superfamily, at least one probability of  $< 10^{-6}$  is obtained. For a collection of 314 families that might potentially be combined,  $(314 \times 313)/2 = 49,141$  comparisons are possible. The probability of finding a score of  $10^{-6}$  by chance in one or more of these is 5%. Thus, we have 95% confidence that all of the families that have been grouped together really share significant sequence similarity.

The ultimate superfamily list could be derived from sequence information alone, provided that at least one sequence was known from most subfamilies within each family. At present we do not have this much sequence information, but often we have information on chemical or physiological functions that reflect relationship. Where we know in advance that several proteins share a similar function, we have required that the probability for a single comparison within the group be < 10<sup>-3</sup> in order to cluster the sequences in the same superfamily.

It is also possible to establish relationships on the basis of search scores (see chapter 1). There are approximately 105 20 residue segments in the data collection, if a segment of 20 residues is compared with all of the 105 ctr ar segments in the collection, an approximately normal distribution of scores is obtained. From the mean and standard deviation of this distribution, the probability of finding a score equal to or greater than any given score can be calculated. In principle, 105 such searches, one for each 20-residue segment, could be performed, leading to the accumulation of  $10^5 \times 10^5 = 10^{10}$  probabilities, If the probability associated with a given score is ≤ 0.5 × 10<sup>-11</sup>. there is a probability of approximately 0.5 X 10<sup>-11</sup> X  $10^{10} = 0.05$  of finding one such score by chance in an exhaustive intercomparison of all segments. The probability of 0.5 × 10<sup>-11</sup> calculated from the normal distribution corresponds to a confidence level of 95% that the sequence similarities discovered by search scores are unusual enough to indicate relationship. We feel that very low probabilities are a reflection of the common evolutionary origin of the proteins. Other similarities of structure, function, and control would therefore be predicted.

### Superfamily Groups

Most of the family relationships in this list were pointed out in the papers describing the sequence work and are referenced in the data pages. Quantitative data on relationships are given in chapter 10 of the Atlas, Volume 5,4 in the Survey of New Material of Supplement 1,5 and in many tables in Supplement 2, as well as in this book. We have applied these quantitative criteria for defining relationship to the suggestions of others and to the hopeful leads that we have turned up by extensive searching of the data in organizing this list.

We have grouped together several proteins of similar function that get borderline probabilities of sequence similarity, including pancreatic hormone from chicken with glucagon and secretin, antibacterial substance A and neocarzinostatin from Streptomyces, ferredoxins with adrenodoxin and putidaredoxin, the fungal with the bacterial ribonucleases, and peanut protease inhibitor and bromelain inhibitor with the Bowman-Birk type protease inhibitors. In other instances we have chosen not to combine borderline cases. The four histones would be combined on the basis of comparisons using the identity matrix but would not be combined using the mutation data matrix. There are a number of short sequences that are repeated in at least two histone groups. However, there have been many insertions and deletions as well as point mutations, so we have left the four groups as separate superfamilies. Human epidermal growth factor (EGF) and a small part of bovine factor X are clearly related. We suspect that EGF may even be a degradation product of

# ORIGINAL PAGE 19 OF POOR QUALITY

an as yet unsequenced serine protease. Because of its distinct function, we have left EGF as a distinct superfamily until the situation is clarified. Bird apovitellenins and the nunan lipid-binding proteins have been left in separate superfamilies. Additional groups of protease inhibitors may eventually be combined when more sequences are known.

Two groups with similar functions and three-dimensional structures do not display significant sequence similarity. The dehydrogenases (alcohol, lactate, glutamate, and glyceraldehyde 3-phosphate) are separate superfamilies, as are the constant and variable regions of the immunoglobulins. Presumably in both of these cases there have been too many insertions, deletions, and point mutations to deduce a common evolutionary origin from the sequences.

Relationships among some of the superfamilies may eventually be demonstrated as more extensive sequence information becomes available for each family, permitting the construction of ancestral sequences for which the mutability of each residue can be estimated. Additional information on relationships may be derived from the similarity of amino acid compositions.

A further organization of superfamilies reflecting common evolutionary origin may be possible based on additional nonsequence information; for example, the three-dimensional structures or the positions in a metabolic pathway. In this list, the superfamilies are grouped according to function or prosthetic group.

It has been estimated that in humans there are approximately 50,000 proteins of functional or medical importance. We conjecture that these will be grouped into about 500 superfamilies, each containing an average of 100 sequences that range from minor variants up to 85% or 90% different from one another. A similar number of superfamilies has been proposed by Zuckerkandl.<sup>6</sup> A landmark of molecular biology will occur when one member of each superfamily has been elucidated. At the present rate of 25 per year, this will take less than 15 years.

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- 3. Dayhof', M.O., Fed. Proc. 35, 2132-2138, 1976
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- Dayhoff, M.O., in Atlas of Protein Sequence and Structure, Vol.5, Suppl.1, ed. Dayhoff, M.O., pp.S1-S8, N.c. Biomed. Res. Found., Washington, D.C., 1973
- 6. Zuckerkandl, E., J. Mol. Evol. 7, 1-57, 1975

### Explanation of Computer Listings of New Entries

We have examined the relationships between all of the new sequences and the ones already in the collection. Each sequence in the Suppl. 3 superfamily list has been assigned five numbers, according to its superfamily number, its position among the families of the superfamily, its position among the subfamilies of its family (paragraphs), its position among the entries of its subfamily (strings separated by semicolons), and its position in the string of sequences in an entry. Each new item has been assigned five numbers that place it between two other entries in the list, where it belongs. We show the first four of these numbers on the updated superfamily list. Thus the first sequence on the list, Cytochrome c-Rice, belongs in the first superfamily and the first family of cytochrome c related proteins. It is in the 14th subfamily, in between the third and fourth entries, sesame and castor. Similarly, the C-phycocyanin alpha chains (No. 5.2) form a new superfamily coming between cytochrome b<sub>562</sub> (No. 5) and ferredoxin (No. 6). Before publication the entire list can be renumbered using only integers, and a superfamily list similar to the one already published can be printed out by the computer.

Some of the new entries contain short sequences or fragments of longer sequences and have not been assigned superfamily numbers. These are listed separately in alphabetical order.

The two computer listings contain 396 items. Of these, 358 are totally new entries, whereas 38 are revisions to published Atlas entries, usually the completion of a sequence for which only fragmentary information was formerly known.

New, complete or almost complete sequences of 20 or more residues with their superfamily classifications

	Cytochrome c	Cytochrome c2	ញ ហ	Rhodospirillum fulvum Cutorbrome C-554	Paracoccus		Synechococcus ATCC 27167 Cutorbrome rA	Synechoco	Cytochrome c551	Ectothiorhodospira halophila		r T		Rhodopseudomonas gelatinosa		Rhodospirillum fulvum	Cytochrome c'	Rhodospirillum molischianum	Cytochrome c'	Rhodospiri		Chromatium vinosum	Cytochrome b5	Rabbit	C-phycocyanin alpha chain	Cyanidium caldariu	_	O)	Mastigocladus lam		Synethococcus sp. (=Anacystis nidulans)		Chiorobium limicola f. sp. thiosulfatophilum Ferradovin		
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30.0	1.0	1.0	1.0	Nuclease (EC 3.1.31.1) precursor Staphulococcus aureus Foooi
31.0	1.0	1.0	2.0	nadius 7P
32. o	1.0	6.0	1.0	1~
32.0	1.0	12.0	1.0	clease kanoaroo
33.0	1.0	J. 5	1.0	  - 
33.0	1.0	2.0	1.0	Lysozyme precursor Chicken
0 . E	1.0	o ci	1.5	Lysozyme Ring-necked pheasant

SUBFAM ENTRY

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						OI OI	RIGIT PC	iai. ' Ior '	PAG QUA	e is					small chain				
Lactalbumin Babbit	Prothrombin Human	Factor IX (Christmas factor)	Bovine Rovine	novine Trypsinogen Sninn doafish	Group-specific protease Rat	Actinidin Chinese gooseberru		7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	ATP pyrophosphatase, lipid-binding protein	Bovine mitocnondrion ATP pyrophosphatase, lipid-binding protein	o m t		atase, coli	ø	isphosphate carboxylase (EC 4.1.1.39)	Enolase (EC 4.2.1.11) Baker's ueast	Tryptophan synthase (EC 4.2.1.20) alpha chain Escherichia coli	Tryptophan synthase (EC 4.2.1.20) alpha chain Salmonella typhimurium	Tryptophanyl tRNA synthetase Bacillus stearothermophilus
1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0 i	1.0
4. 0	i 0	1.0	1.0	о О	1.0	0.1	1.0	1.0	1.0	o ni	э. о	1.0	1.0	1.0	1.0	J. 0	1.0	1.0	1.0
5.0	1.0	1.5	ານ ເນ	4.0	6.5	0.0	0.e	1.0	1.0	1.0	1.0	5.0	о е	4.0	1.0	1.0	1.0	1.0	1.0
33.0	39.0	39.0	39.0	39.0	39.0	41.0	47.0	47.2	47.4	47. 4	47.4	47. 4	47. 4	47.4	47.6	49.5	50.0	50.0	52. 2

SUBFAM

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## ORIGINAL PAGE 19 OF POOR QUALITY

											Ur	POU.	n V	UAL						
	D-erythrodihydroneopterin triphosphate synthetase Rat, quinea pig, and bovine	×	Beta-1 bungarotoxin B chain, major component	Beta-1 bungarotoxin B chain, minor component Formosan handed krait	Basic protease inhibitor Red sea turtle		Ovomucoid (PSTI-type protease inhibitor) Turkeu	Ovomucoid (PSTI-type protease inhibitor) precursor Chicken	Plasminostreptin (PSTI-type protease inhibitor) Streptomuces antifibrinoluticus	Ovalbumin Chicken	<b>~</b>	protease inhibitors (Bowman-Birk) Adzuki hean	Proteinase inhibitor	Eggplant Somatomedin B	pept	rig, bovine, and sneep Corticotropin-lipotropin precursor Rovine	Beta-endorphin II Chum salmon	Thyrotropin alpha chain Human	Lutropin alpha chain Human	Follitropin alpha chain Horse
ENTRY	1.0	1.0	1.0	2.0	1.0	1.0	0	က် ဝ	1.0	1.0	1.0	2.0	1.0	1.0	1.0	1.0	5.0	1.0	1.0	4.0
SUBFAM	1.0	က က	1.0	1.0	1.0	1.0	1.0	1.0	o તાં	1.0	1.0	5.0	1.0	1.0	1.0	1.0	o .c	1.0	1.0	1.0
FAM	1.0	ი ი		ល	5.0	5	4.0	4.0	ις ()	2.0	1.0	1.0	1,0	1.0	1.0	1.0	ю. О	1.0	1.0	1.0
SUPFAM	52. B	53.0	53.0	53.0	53.0	54.0	54.0	54.0	54.0	55.0	55. 5	58.0	62.5	63.5	64.5	65.0	65.0	99.99	66.0	66.0

Lutropin alpha chain	norse Thyrotropin beta chain Human	Follitropin beta chain	Follitropin beta chain	Prolactin	numan Prolactin precursor pot	somatotropin precursor Rat	Insulin	1 ( 1 (	rercupine Insulin	Casıragua Egg-laying hormone Ect hare	boxin 1	sed snak otoxin 2 cox cox	a shake (mstrutia stukesi Xin 1	Australian tiger snake Venom protein S2C4	Jameson's mamba Venom protein CM-11	ptian cobra	Short venom protein DE1 King cobra	ید ب	Short toxin CM-2	Egyptian cobra Short neurotoxin 1 Mozambique cobra
4.0	1.0	0 6	3.0	1.0	1.0		1.3	1.6	2.0	1.0	1.0	ان 0	1.0	1.0	ດ່		o m	1.0	1.0	7.5
1.0	1.0	1.0	1.0	0.5	9. o	1.0	1.0	1.0	3.0	1.0	છ	5	4.5	1.0	1.0	1	1.0	1.0	1.0	0 ë
1.0	1.0	2.0	2.0	1.0	1.0	о 0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	4. H	4		4.	4.3	4.6	5.0
66.0	67.0	67.0	67.0	68.0	68.0	68.0	75.0	75.0	75.0	77.5	78.0	78.0	78.0	78.0	78.0	i 1	78.0	78.0	78.0	78.0

SUBFAM

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78.0	5.0	9.0	7.7	Short neurotoxin 3 Mozambique cobra	
	5.0	5.0	3.0	Short neurotoxin 1 Stokes' sea snake (Astrotia stokesii)	
	6.0	1.0	11.5	n S an cobra	
	1.0	1.0	ن ن ن	toxin a	
	1.0	1.0	3.0	ide C	
	1.0	2.0	1.0	pacific rattlesnake III	
	5.0	ان ن	1.0	Scorpion (Androctonus australis) Neurotoxin V	
	ы 0	o 6	1.0	_	
	1.0	2.0	1.0	Scorpion (Buthus eupeus) Toxin I	
	1.0	1.0	1.0	Sea anemone (Anemonia sulcata) Toxin III	
	(	,			
	o ir	1.0	ວ ຫໍ	Purotnionin 11 Barleu	
	1.0	0 તાં	9.5	Ig kappa chain V-I region Human Kue	
	1.0	က က	1.0	Ig kappa chain V—II region Dog Gom	
	1.0	بي ت	1.0		
•	1.0	6.5	1.0	Ig kappa chain precursor V region Mouse K2 gene translation	
	1.0	6.5	0 0	schain p K3 cene	
	1.0	9.0	2.0	a chain p MOPG 323	
	1.0	9.0	0 ë	a chai CBPC.	
	1.0	9.5	1.0	Ig kappa chain V regions Mouse X-44	
	1.0	16.0	5.0	Ig kappa chain V region Rabbit K29-213	

SUBFAM ENTRY

FAM

Ig lambda chain V-II region Human Bur	•	Ig lambda chain V-IV region Human Hil	Ig lambda chain V-VI region Human Nig-48	Ig lambda-2 chain precursor V region Mouse	Ig heavy chain V-III region Human Hil	Ig heavy chain V region Mouse X24	Ig heavy chain'V region Mouse J539	Ig heavy chain V region		Š	Ig heavy chain V-III region Human Dob	- <b>-</b>		Ia-2 c	a-3 he	2-6	Ig gamma-1 chain C region Mouse	Ig mu chain V and C regions Mouse MOPC 104E	Ig mu chain V-III region and fragment of C region Dog Moo (fragments)
0 હાં	1.0	1.0	1.0	0.0	1.0	2.0	ဝ ຕ່	Ö. Ö.	4.0	1.0	1.0	1.0	1.0	1.0	2.0	1.0	૦ તાં	1.0	1.0
g. 0	7.5	9.0	11.5	1.0	1.5	8.0	8. O	B. 0	8.0	g. 0	10.5	12.5	o ::	0 6	1.0	<u>က</u> က	4. 0	5.0	0
5.0	5.0	o .c	0	о Э. о	7.0	.7.0	7.0	7.0	7.0	7.0	7.0	7.0	1.0	i 0	4.0	4.0	4.0	5.0	5.0
88.0	8B. 0	88.0	88.0	88.0	88.0	88.0	88. 0	88.0	88. 0	88.0	88.0	88.0	89.0.	89.0	89.0	89.0	89.0	89.0	89.0

FAM SUBFAM

	Ig alpha-2 chain V-III and C regions, A2m(2) allotype Human But	Ig alpha-2 chain C region, A2m(1) allotype Human Lan	Ig alpha-1 chain V and C regions Mouse MOPC 47A	Beta-2 microglobulin Rabbit	Histocompatability antigen HLA-B7 heavy chain Human (franment)	Hemoglobin alpha chain Brown lemur	Hemoglobin alpha chain Tracebren	Hemoglobin alpha chain Guinea oio	מו ויייני		Hemoglobin alpha chain Llama and Arabian camel	bin a	Hemoglobin alpha chain (stress-induced)	Hemoglobin alpha chain	Grayiay yoosa Hemoglobin pi chains Chirken embruo	Hemoglobin delta chain Human, chimpanzee, gorilla, and gibbon	in beta chain lemur	Hemoglobin beta chain Treeshrew	Hemoglobin beta chain Guinea pio	עו דייי
ENTRY	5.0	5.0	1.0	1.0	1.0	2.5	4.5	6. 5	7.5	g. 5	10.0	11.0	1.5	2.0	1.0	2.0	4. S	ឆ . ឆ .	9.5	9.5
SUBFAM	1.0	1.0	2.0	P. O.	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	5.0	5.0	5.5	1.0	1.0.	1.0	1.0	1.0
FAM	ა. ა	6.0	6.0	7.0	8.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	o.e	ဝ ဗ်	o Ö	o ဗ်	9. O
SUPFAM	89.0	89.0	89.0	89.0	89.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0

Hemoglobin beta chain Big	globin g	Hemoglobin beta chain		Greylay yoose Hemoglobin beta chain Carn	Hemoglobin beta chain Port larkeon chark	oin Sin	יים מבים	Myaglabin	ממר א שטוו	River lamprey Globin III		Globin CTT-II beta	ູ່ບ	ູ່ບ	ູ່ບຸ	Midge tarva Globin CTT-X Midge larva	, כי		Leghemoglabin II Yellow lupin
14.0	1.0	1.0	2.0	1.0	1.0	7.5	40.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	5.0	o તાં
1.0	2.0		5.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	. 2. 0	0.6	4.0	5.0 ·	1.0	3.0	4.0
0 	ဝ ဗ	0 6	ဝ က်	е; т	ଧ ଜ	4.0	4.0	4.5	5.0	ຸດ ເນ	B	9.0	9.0	9.0	9.0	9.0	10.0	11.0	11.0
90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0	90.0

SUBFAM ENTRY

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Histone Hi.3 Rabbit	Histone H1 Trout	Histone H1, gonadal Sea urchin (Parechinus annulosus)		Histone H2A	Chicken Histone H2A, gonadal Sea urchin (Psammechinus miliaris)	embryonic s	Histone H2B Bovine and human .	H2B trout	4:	HZB	Fruit fly	Sea urchin	=	e H2B(2), sperm	sea urchin (Pärechinus angulosus) Histone H2B(3), sperm	Sea urchin (Pa	Histone H3, embryonic Sea urrhins	Nonhistone chromosomal protein HMG-17		Nonnistone cnromosomal protein HMG-1/ Chicken	Nonhistone chromosomal protein H6 Rainbow trout	Protamine (stellin.A) Sturgeon (Acipenser stellatus)
1.0	1.0	й. 0	1.0	1.0	о ю	4.0	1.0	2.0	1.0	0	7	<b>;</b>	1.0	1,0	1.0		1.0	1.0		o ก่	1.0	O ++
1.0	0 i	э. о	1.0	1.0	1.0	1.0	1.0	1.0	0 6	5.0	Ç	o i	4.0	5.0	р О	 	1.0	1.0	,	o.i	5.0	រប ភេ
1.0	1.0	1.0	6.0	G.:	1.0	1.0	1.0	1.0	1.0	1.0	,	·;	1.0	1.0	0	! •	1.0	1.0	!	1.0	1.0	1.0
91.5	91.5	91.5	91.5	92.0	, 92, 0	92.0	93.0	93.0	93.0	93.0	(	) , ,	93.0	93.0	0 0 0	1 1	94.0	95. B		95. B	95.8	99.0

SUBFAM ENTRY

FAM

100.2	1.0	1.0	1.0	DNA-binding protein NS1 Ferbarichia roli
100.2	i. 0	2.0	1.0	ים. זכה ת
100. 2	رن 0	1.0	1.0	rotein unidoski
100.3	1.0	1.0	1.0	Initiation factor IF-1 Ferborichia coli
100.4	1.0	1.0	1.0	tion fa
100. 6	1.0	1.0	1.0	-
100.7	1.0	1.0	1.0	
100.9	1.0	1.0	1.0	Castor bean . 305 ribosomal protein 53 Errhomichin roli
101.5	1.0	1.0	1.0	30S ribosomal protein S5
102.5	1.0	1.0	1.0	col pro
108.2	1.0	1.0	1.0	
109.5	1.0	1.0	1.0	Escherichia coli 305 ribosomal protein 519 Eschonichia coli
111.7	1.0	1.0	1.0	ribosomal pro
111.9	1.0	1.0	1.0	stileritiis tui ribosomal pro erboxithia rol
112.5	0.	1.0	1.0	ribosomal
113.0	1.0	o i	1.0	ribosomal
113.5	1.0	1.0	1.0	ribosomal Pibosomal
114.1	1.0	1.0	1.0	
114.4	1.0	1.0	1.0	ribosomal scherichia
114.5	1.0	1.0	1.0	ribosomal scherichia

SUBFAM

FAM

50S ribosomal protein L15 Ferberichia roli	ribosomal srherichia	Ribosomal pro erhenichia col	ribosomal pro srbarichia col	ribosomal pro	107	ribosomal pro arbarichia rol	ort lemosour ortherichia	Ribosomal pro		Structural protein VP2	دد	al T (tumor)	(tumor) Virus	agglutinin p owl influenz	t protein acterioohage 1	t protein	olatory protein O arterionhane lambda	ulatory prote arterioohade	latory prote cteriophage
1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	10	1.0	1.0
1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	ن 0.	1.0	9.0	o .e	1.0	1.0	1.0
114.8	116.2	<u>1</u> 16.3	116.4	116.7	116.8	118.5	120.5	123.1	123. 2	123. 3	123.3	123.4	123.4	123.8	127.0	128.0	128. 2	128.3	128.4

SUBFAM

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n b d a	tein osis virus	protein	II , T2, And T6	74			i-X174					phi-X174				i-X174					i-X174		chain, minor component	
Repressor protein Bartariophage lambda	lusion bod uclear pol	Small outer capsid Bacteriophage T4	Internal peptide VII Bacterioohage T4,	p T	e A and A* pr acteriophage	Genz B protein Bacteriophage G4	Gene C protein Bacteriophage phi	O)	Gene D protein Rarterionhane 94	li l	cte	Gene r protein Bacteriophage phi	u.	G protein	H protein	a		Bacteriophage G4 Cana . I protain	cterioph	F	Bacteriophage phi	Gene K protein Barteriophage G4	crystallin crystallin	Kat
1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	2.0	1.0	,	1.0	1.0	1.0	1.0		1.0	<b>C</b>	;	1.0		1.0	ળ	
1.0	1.0	1.0	1.0	2.0	0 i	0 5 0	1.0	5.0	1.0	2.0	. (	F. O	0 i	1.0	1.0		2.0	7	; ;	1.0		2.0	1.0	
1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0			1.0	0 ii	1.0		1.0	ŗ	o i	1.0		1.0	1.0	
128.5	129.4	131.2	131.3	131.8	131.8	132.0	132.1	132. 1	133.0	134.0	1	134. 5	134.5	135.0	135.5		135.5	C T	120.0	136.1		136. 1	138.0	

SUBFAM

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Tropomyosin alpha chain, skeletal muscle Rabbit	Tropomyasin beta chain, skeletal muscle Rabbit	Actin Rabbit	Actin Phusanum nolurenhalum	profilin Bovine	Myosin DTNB light chain, skeletal muscle Rabbit	Myosin DTNB light chain, skeletal muscle Chicken	Myosin EDTA light chain Scallop	Parvalbumin beta Coelacanth	Parvalbumin alpha	Calcium-binding protein, intestinal	S-100 protein	I, sk	Troponin I, slow skeletal muscle Rabbit	Lipid-binding protein C-II Human	Apovitellenin I	Neurophysin 1 Pia	Complement C3a anaphylatoxin Rat	Complement C5a anaphylatoxin Human	J chain Human
1.0	0.0	1.0	i 0	1.0	1.0	o ; .	£. 0	1.0	1.0	1.0	1.0	5.0	1.0	1.0	0.9	0 i	1.0	1.0	1.0
1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	6. 5	8.0	1.0	1.0	1:0	1.5	1.0	2.0	1.0	3.0	1.0	1.0
1.0	1.0	1.0	1.0	1.0	4.0	4.0	4.5	5.0	5.0	6.0	7.0	1.0	1.0	က က	1.0	1.0	1.0	5.0	1.0
146.0	146.0	147.0	147.0	147.2	148.0	148.0	148.0	148.0	148.0	1.48. 0	148.0	150.0	150.0	151.0	152.0	160.0	167.0	167.0	167.2

SUBFAM

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Beta-thromboglobulin Human	Platelet factor 4 Human	Uteroglobin precursor Rabbit	Gamma-carboxyglutamic acid-containing protein Swordfish	Metallothionein-1A	Metallothionein-2	roman Metallothionein-I Monse	thione	neurospora crassa · Proline-rich phosphoprotein A	Retinol-binding protein	15 S F	(Antheraea polyphemu ass B protein pc10	oth (Anth -rich pep		Honey bee Sillucin	Mucor pusillus Favin alpha chain	roz tir	Pea Favin beta chain Dand koma	rodu beam umatin I Facerate	inaumatococcus danieilli Citrate lyase acyl carrier protein Klebsiella aerogenes
1.0	1.0	1.0	1.0	0.5	2.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0 i	1.0	1.0	1.0
1.0	1.0	1.0	1.0	1.0	1.0	5.0	1.0	1.0	1.0	1.0	o oi	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
1.0	o 6	1.0	o તાં	1.0	1.0	1.0	ن ن	1.0	1.0	1.0	0.1	1.0	1.0	1.0	9.0	2.0	တ တ	1.0	1.0
169.2	169.2	169.4	170.0	171.0	171.0	171.0	171.0	172.1	172.2	173.5	173.5	173.6	174.2	174.5	175.0	175.0	175.0	179.5	180.1

SUBFAM

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SUPFAM

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	Biotin carboxyl carrier protein (in EC 2.1.3.1) Propionibacterium shermanii	Phosphocarrier protein HPr Stanhulococcus aureus	LIV-binding protein Escherichia coli	Outer membrane protein Ia Escherichia coli B/r	L-Arabinose-binding protein Escherichia coli	Bacteriorhodopsin Halobacterium halobium	Spore protein A Racillus menaterium	Lactose permease Escherichia coli
ENTRY	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
SUBFAM	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
FAM	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
SUPFAM	180.2	180.4	180.6	180.7	180.8	181, 2	181.4	182. 1

Total Number of Sequences:

348

# Alphabetical listing of other new entries

2-Keto-3-deoxy-6-phosphogluconic aldolase Pseudomonas putida (fragment)

3-Oxoadipate enol-lactonase II Acinetobacter calcoaceticus (fragment)

Alpha-1-antitrypsin Human (fragment) Alpha-amylase (EC 3.2.1.1) Bacillus amyloliquefaciens (fragment) Aminopeptidase I alpha chain Bacillus stearothermophilus (fragment)

Anthranilate phosphoribosyltransferase Serratia marcescens (fragment)

Anthranilate phosphoribosyltransferase Erwinia caratovora (fragment)

Anthranilate synthase, component I Escherichia coli (fragment) Anthranilate synthase, component II Escherichia coli (fragment) Aspartate carbamoyltransferase C chain Escherichia coli (fragment)

Beta-endorphin I Chum salmon Biotin carboxyl carrier protein (in EC 6.4.1.2) Escherichia coli (fragment)

Carboxyl protease Mucor miehei (fragments)

Ceruloplasmin Human (fragment)

Coagulogen Japanese horseshoe crab (fragment)

Corticotropin-lipotropin precursor Pig (fragment)

Greating kinase Rabbit (fragment) D-Serine dehydratase Escherichia coli (fragments) Factor XIII (EC 2.3.2.10) a chain Human (fragment)

Fructose bisphosphatase Rabbit (fragment) Glucose-1-phosphate adenylyltransferase Escherichia coli B (fragment)

Gonadotropin alpha chain Carp (fragments)

Gonadotropin beta chain Carp (fragments) Hemoglobin epsilon chain Homan (fragments) Histidine decarboxylase small chain Micrococcus sp. (fragment) Histocompatability antigen H-2Kb heavy chain Mouse (fragment) Histocompatability antigen HLA-A2 heavy chain Human (fragment)

Histone H2A1 Wheat germ (fragment)

Histone H2A2 Wheat germ (fragment)

Histone H2A3 Wheat germ (fragment) Histone H2B African crocodile (fragments)

Histone H2B Chicken (fragments) Histone H2B South African toad (fragments) Histone H4 Tetrahymena thermophila (fragments)

Histone H5 Pigeon (fragment) Indoleglycerol phosphate synthase Escherichia coli (fragment) Inter-alpha-trypsin inhibitor (BPI-type) Human (fragment)

Isomaltase Rabbit (fragment)

Lectin

Limulin Horseshoe crab (fragment)

Lentil (fragments)

Lipotropin beta (and beta-endorphin) Mouse (fragment) Macromomycin Streptomyces macromomyceticus (fragment)

Myelin P2 protein Rabbit (fragment) Ribonuclease (colicin E3, A chain) Escherichia coli plasmid (fragment)

Ú

Ribulose-1,5-bisphosphate carboxylase (EC 4.1.1.39) Chlamydomonas reinhardtii (fragment)

Serum albumin precursor Rat (fragments) Transaminase B (EC 2.6.1.32) Escherichia coli (fragment) Triacylglycerol lipase (EC 3.1.1.3) Pig (fragment) Total Number of Sequences:

48

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